stenosis despite a conservative approach to asymptomatic carotid disease, in keeping with previous studies.[1,4] Following a transient ischemic attack, patients require duplex scanning after the event to direct their management. Thus, for patients in whom a conservative approach is to be applied to asymptomatic restenosis or progression of contralateral disease, the value of duplex surveillance is limited to research and audit. To clearly demonstrate a value of duplex surveillance following carotid surgery would require an appropriately powered randomized trial. Possibly more useful than duplex surveillance might be the identification of biomarkers, genetic markers or new imaging techniques that better identify presently asymptomatic patients likely to experience a stroke.[5,6]

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Reply

We appreciate professor Golledge's comments on one of the more controversial issues concerning patients who undergo carotid surgery—ie, the utility of ultrasound surveillance to manage the progression of contralateral asymptomatic carotid disease.[1]

Golledge asserts that "an imaging finding is primarily of value if it alters the clinical management of the patient." Therefore, taking Golledge's words literally, because diabetic patients (being at high vascular risk, according to current guidelines) are given antiplatelet therapy, they should not have duplex ultrasonography (DUS) until they suffer a stroke or other cardiovascular event, because it is only then that a change of treatment would be recommended—a bit late, in our opinion. According to the results of the major randomized clinical trials, DUS follow-up would at least pinpoint patients progressing to severe asymptomatic carotid disease and likely to benefit from carotid endarterectomy. Contrarily to the previous statement, Golledge himself admits that DUS can noninvasively detect patients with complications potentially hazardous to their health if not properly treated.

Golledge says that "ipsilateral restenosis. . .is believed to have a benign natural history and therefore many clinicians treat such lesions medically."[2] But how do we identify ipsilateral restenosis without proper imaging? And how can the benign nature of such lesion be established without a proper follow-up, including clinical assessment and instrumental evaluation (DUS is the cheapest and safest method available)?

The meta-analyses that Golledge mentions[3,4] demonstrate that, in expert hands, patients (especially men) with stenosis greater than 60% clearly benefit from carotid endarterectomy; considering the burden of stroke on a patient and the community, we are sure Golledge would agree on the merits of avoiding even a single stroke.

We agree that an appropriately powered randomized trial would be preferable to our large but single-center study, and we would be happy to collaborate with professor Golledge to set up such a trial. Every patient deserves the best possible management, wherever they live, which is why DUS (which is readily available everywhere, cheap, and noninvasive) is useful in such a context (the same can be hardly be said for the high-resolution, ultrasmall, superparamagnetic iron oxide–enhanced magnetic resonance imaging[5]). We know of no specific biomarkers or genetic markers capable of reliably identifying asymptomatic patients likely to experience a stroke: C-reactive protein is one of many biomarkers being studied as a predictor of cardiovascular events in patients with carotid stenosis[6], but it is aspecific for stroke, and the research has been conducted on patients taking platelet inhibitors and/or statins, which influence not only the occurrence of cardiocerebrovascular events but also the levels of acute-phase inflammatory parameters such as C-reactive protein.

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Regarding "EXCLUDER trial events are excluded from EXCLUDER trial report"

We read with interest the article of Peterson et al,[1] which reported 5-year data from a controlled trial of the EXCLUDER device for endovascular repair (EVAR) of abdominal aortic aneurysms but are concerned that their conclusions are not supported by the presented data. The study was nonrandomized, as the investigators state, but there are other large sources of confusion. For example, of 235 patients selected for EVAR, only 128 patients are included with no explanation of what happened to the remaining 107 patients. Furthermore, though the investigator's definition of adverse events is given in text, there is no description of what these events actually were, who adjudicated them, or whether they were blinded. The authors show that nearly 70% of patients treated with open repair had a major adverse event within 30 days,

a rate that seems preposterously high. If that is so, how can that group have had a survival rate that is as good or better than the EVAR group? These sources of confusion, as well as a lack of disclosure of what the major adverse events actually were, lead us to conclude that the study *does not show* anything specific about EVAR with the EXCLUDER device or that it has "fewer major adverse events compared with open repair."

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doi:10.1016/j.jvs.2007.07.045

Reply

We are pleased that Drs McMurtry and Beckman were interested in the 5-year report[1] and appreciate the opportunity to respond. Of the original 235 test patients, 128 entered the final 5-year interval. The 107 test patients that were not available included 54 patients who died, 30 patients who withdrew consent, and 23 patients who were unavailable for other reasons. Those with experience performing these long-term studies recognize the difficulties of retaining enrollment of these elderly patients with considerable medical problems. The original power analysis anticipated a 6.5% annual mortality and 8% annual lost to follow-up. In retrospect, these predictions were remarkably accurate, although we had fewer patients lost to follow-up than predicted due to the conscientious work of the site coordinators and investigators. Despite the attrition, there were enough subjects in each group to show a statistically significant difference between test and control arms in freedom from any major adverse event after 5 years.

Many of your "other large sources of confusion" can be clarified by reading the previously published and referenced 2-year results.[2] Specifically, "adverse events were stratified by severity into minor and major adverse events by published criteria, and this stratification was reviewed by a Clinical Events Committee." Further details on the criteria for adjudication and the categories of these early events are provided in the methods section and Table IV. Categories of later major adverse events are given in the Table below. The Clinical Events Committee was a multispecialty group that was blinded as much as possible and applied reporting standards published at the time of study initiation–the Sacks criteria.[3] The blinding process helps avoid biased adjudication of adverse events as your comment on "preposterously high" reveals that there are clearly preconceived biases of the safety of the control treatment. As detailed in the discussion, further analysis of minor, major, and total complications was performed to determine whether the Sacks criteria obscured differences between groups. There were significantly fewer complications in the test group regardless of the stratification by severity. In fact, the early major adverse event rates using these published criteria were 14% of test group vs 57% of control group, not "nearly 70%" that you claim. The nonrandomized nature of this trial is a limitation that was addressed by performing a multivariable analysis including known differences in the two groups. This showed that test group was still a strong independent predictor for fewer major adverse events.

Your query regarding the difference in major adverse events not being associated with differences in mortality is simply answered by the reality that vascular surgeons recognize and treat postoperative complications effectively. These adverse events often prolong hospitalization and recovery as was demonstrated in differences in clinical utility, but fortunately do not often lead to mortality.

The goal of this 5-year report was not to reiterate findings previously found in the 2-year results, but rather to determine if reinterventions and late events in the test group resulted in loss of the early benefits seen after endovascular abdominal aortic aneurysm repair. We stand by our conclusions that after 5 years, endovascular repair has fewer major adverse events despite including late reinterventions when compared with open repair.

Sincerely,

Table. Categories of late major adverse events

	Year 1-after 30 d		*Year 2*		*Year 3*		*Year 4*		*Year 5*	
	Test	*Control*	*Test*	*Control*	*Test*	*Control*	*Test*	*Control*	*Test*	*Control*
Subjects evaluable	232	97	213	82	185	71	161	61	128	47
Subjects with one or more MAE	68	23	55	15	33	8	29	15	15	5
Bleeding complications	1	—	1	—	1	—	3	1	—	—
Endoleak requiring intervention	13	—	10	—	2	—	3	—	—	—
Pulmonary complications	10	4	4	2	5	1	7	4	4	1
Cardiac complications	16	13	18	8	11	3	6	8	7	3
Genitourinary complications	6	2	—	—	—	—	3	—	1	—
Sepsis	1	—	—	—	1	—	1	—	—	—
Neoplasm	7	1	8	2	5	3	4	—	—	—
Renal complications	5	—	4	1	3	1	2	3	1	—
Wound complications	8	3	1	1	2	2	1	1	—	—
Bowel complications	8	3	7	1	2	1	2	2	1	1
Vascular complications	7	4	1	2	2	—	2	—	1	1
Neurologic complications	8	5	6	1	4	—	2	2	1	—
Other complications	12	2	11	3	8	1	7	3	1	—
Death (unknown cause)	—	—	—	—	—	—	1	—	—	—
Increase in aneurysm requiring intervention (with or without endoleak)	1	—	8	—	1	—	6	—	2	—

MAE, Major adverse events.